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L4            12 S L3

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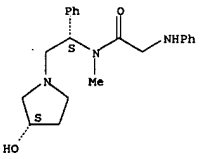
L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1341978 CAPLUS
DN 144:232878
TI Novel phenylamino acetamide derivatives as potent and selective κ opioid receptor agonists
AU Chu, Guo-Hua; Gu, Minghua; Cassel, Joel A.; Belanger, Serge; Stabley, Gabriel. J.; DeHaven, Robert N.; Conway-James, Nathalie; Koblish, Mike; Little, Patrick J.; DeHaven-Hudkins, Diane L.; Dolle, Roland E.
CS Department of Chemistry, Adolor Corporation, Exton, PA, 19341, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(3), 645-648
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
AB A novel series of phenylaminoacetamide derivs. was synthesized. These amides were shown to be potent and selective κ opioid receptor agonists.
IT 851679-94-2P 851679-95-3P 851679-96-4P
851679-98-6P 851679-99-7P 851680-00-7P
851680-03-0P 851680-08-5P 851680-15-4P
851680-16-5P 851680-17-6P 851680-19-8P
851680-21-2P 851680-22-3P 851680-26-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of N-[3-hydroxypyrrolidinyl(phenyl)ethyl]phenylaminoacetamides as potent and selective κ opioid receptor agonists)

RN 851679-94-2 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-(phenylamino)- (9CI) (CA INDEX NAME)

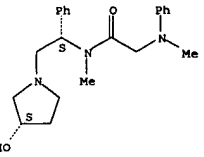
Absolute stereochemistry.



RN 851679-95-3 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-(methylphenylamino)- (9CI) (CA INDEX NAME)

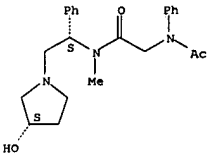
Absolute stereochemistry.

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



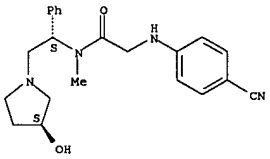
RN 851679-96-4 CAPLUS
CN Acetamide, 2-(acetylphenylamino)-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851679-98-6 CAPLUS
CN Acetamide, 2-[(4-cyanophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

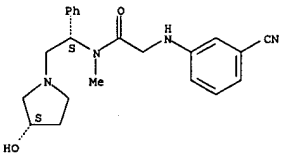
Absolute stereochemistry.



RN 851679-99-7 CAPLUS
CN Acetamide, 2-[(3-cyanophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

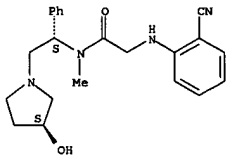
L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



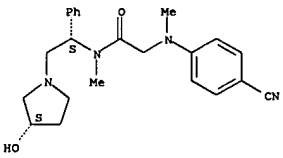
RN 851680-00-7 CAPLUS
CN Acetamide, 2-[(2-cyanophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851680-03-0 CAPLUS
CN Acetamide, 2-[(4-cyanophenyl)methylamino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

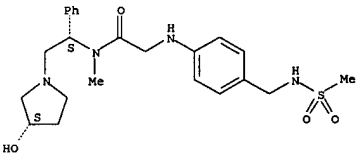
Absolute stereochemistry.



RN 851680-08-5 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-[[(methylsulfonyl)amino]methyl]phenyl]amino]- (9CI) (CA INDEX NAME)

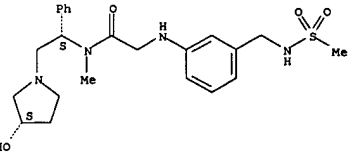
Absolute stereochemistry.

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



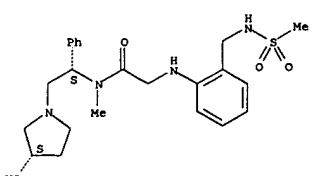
RN 851680-15-4 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[3-[[(methylsulfonyl)amino]methyl]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



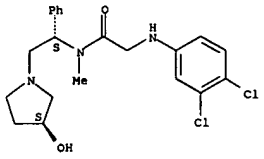
RN 851680-16-5 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[2-[[(methylsulfonyl)amino]methyl]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



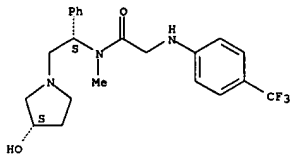
RN 851680-17-6 CAPLUS
CN Acetamide, 2-[(3,4-dichlorophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



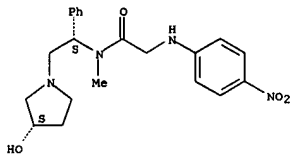
RN 851680-19-8 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-(trifluoromethyl)phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851680-21-2 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[(4-nitrophenyl)amino]- (9CI) (CA INDEX NAME)

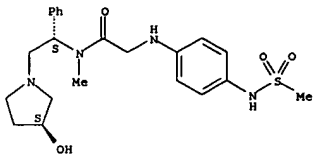
Absolute stereochemistry.



RN 851680-22-3 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-[(methylsulfonyl)amino]phenyl]amino]- (9CI) (CA INDEX NAME)

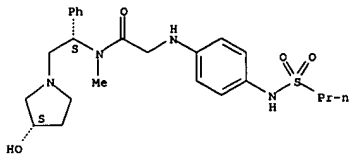
L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



RN 851680-26-7 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-[(propylsulfonyl)amino]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1242315 CAPLUS
DN 143:477661
TI Preparation of cyclohexyldiamine derivatives as modulators of ORL1 receptors
IN Sundermann, Corinna; Sundermann, Bernd
PA Gruenenthal G.m.b.H., Germany
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| PI WO 2005110974 | A1 | 20051124 | WO 2005-EP4913 | 20050506 |
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| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 102004023522 | A1 | 20051201 | DE 2004-102004023522 | 20040510 |
| PRAI DE 2004-102004023522 | A | 20040510 | | |

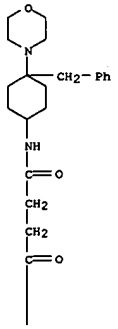
OS MARPAT 143:477661
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

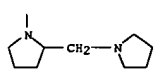
AB Title compds. I [n = 1-5; R1 and R2 independently = H, (un)substituted alkyl, cycloalkyl, etc. or R1 and R2 together may form CH2CH2OCH2CH2, CH2CH2NR6CH2CH2 or (CH2)3-6; R6 = H, (un)substituted alkyl, aryl, etc.; R3 = (un)substituted alkyl, cycloalkyl, heteroaryl, etc.; R4 = -(CR7R8)pR9; p = 0-4; R7 = H or (un)substituted alkyl; R8 = H, (un)substituted alkyl and COOR10 or R7 and R8 together may form ring (CH2)yCHR9(CH2)m; y = 1-3; m = 1-2; R9 = (un)substituted alkyl, aryl, heteroaryl, etc.; R10 = H or alkyl; R5 = H or -(CH2)xR9 or together with R4 may form CH2CHR11OCHR11CH2, CH2CH2SCH2CH2, CH2CH2NR12CH2CH2, etc.; R11 = H or (un)substituted alkyl; R12 = H, (un)substituted alkyl, cycloalkyl, etc.; x = 1-3] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of ORL1 receptors. Thus, e.g., II was prepared by coupling of 4-[2-(4-chlorophenyl)ethyl-carbamoyl]butyric acid with 4-benzyl-4-dimethylaminocyclohexanone and subsequent conversion into the hydrochloride. The binding activity of I towards ORL1 receptors was evaluated in scintillation assays using recombinant CHO-ORL1 cells and it was revealed that selected compds. of the invention displayed binding activity in the range of 39 up to 100%. I as modulator of ORL1 receptors should prove useful in the treatment of obesity, depression and pain. Pharmaceutical compns. comprising I are disclosed.

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 869745-94-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclohexyldiamine derivs. as modulators of ORL1 receptors)
RN 869745-94-8 CAPLUS
CN 1-Pyrrolidinebutanamide, N-[4-(4-morpholinyl)-4-(phenylmethyl)cyclohexyl]-γ-oxo-2-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



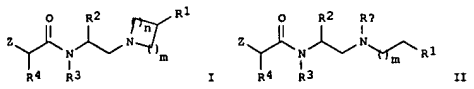
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:431398 CAPLUS
DN 142:463595
TI Preparation of N-aminoalkyl amides as agonists of the κ opioid receptor useful against gastrointestinal disorders, pain, and pruritus
IN Dolle, Roland E.; Chu, Guo-Hua; Gu, Minghua
PA USA
SO U.S. Pat. Appl. Publ., 46 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

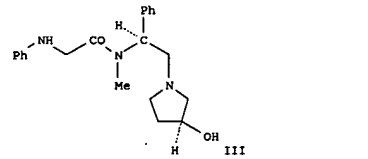
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2005107355 | A1 | 20050519 | US 2003-713746 | 20031114 |
| WO 2005049564 | A1 | 20050602 | WO 2004-US37955 | 20041112 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-713746 A 20031114
OS MARPAT 142:463595
GI


I


II


III

AB Amide derivs. (shown as I and II; variables defined below; e.g. N-[2-((S)-3-hydroxypyrrolidin-1-yl)-(S)-1-phenylethyl]-N-methyl-2-phenylaminoacetamide (shown as III)) are disclosed. Pharmaceutical compns. contg. these compds., and methods for their use, inter alia, for treating and/or preventing gastrointestinal disorders, pain, and pruritus (no data) are also disclosed. Although the methods of prepn. are not claimed, 36 example prepns. are included. For example, III was prepd. (45 %) by coupling of N-phenylglycine with N-{2-((S)-3-hydroxypyrrolidin-1-yl)-(S)-1-phenylethyl}-N-methylamine dihydrochloride. For I and II: R1 is H or OH; Ra is alkyl; R2 is alkyl, aryl, or aralkyl; R3 is alkyl, or R2 and R3 taken together with the atoms through which they are connected form a 4- to 8-membered heterocyclic ring; R4 is H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl, heteroaryl, or heteroarylalkyl; Z is -(CH2)oNR5R6 or -(CH2)oC(:O)NR7R8; R5 is H, alkyl, or aryl; R6 is aryl, alkaryl, -CO(NH)pR9, or -SO2R9, provided that at least one of R5 and R6 is other than aryl; R7 is H or alkyl; R8 is alkyl, aryl, aralkyl, alkaryl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl; R9 is alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl, heteroaryl, or heteroarylalkyl; m is the integer 1, 2, or 3; n is the integer 1, 2, or 3; o is the integer 0, 1, 2, or 3; p is the integer 0 or 1; and the quantity (m+n) is an integer 2-5. Compds. in all the examples showed κ receptor affinity (Ki) <10 μM. For example, III had a Ki = 0.17 nM against the human κ receptor with >100+ selectivity vs. the human μ and δ receptors and was an agonist with an EC50 = 0.05 nM. It exhibited a % A = 96.2% at a dose of 300 μg, i.paw in the in vivo formalin-induced nociception assay. This compd. also blocked the action of HOAc-induced writhing when administered s.c. with an ED50 = 0.017 mg/kg.

IT 851679-94-2P 851679-95-3P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-2-[methyl(phenyl)amino]acetamide 851679-96-4P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-2-[acetyl(phenyl)amino]acetamide 851679-98-6P, 2-(4-Cyanophenylamino)-N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide 851679-99-7P, 2-(3-Cyanophenylamino)-N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide 851680-00-7P, 2-(2-Cyanophenylamino)-N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide 851680-01-8P, 2-[(4-Aminomethylphenyl)amino]-N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide hydrochloride 851680-03-0P, 2-[(4-Cyanophenyl)(methyl)amino]-N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide 851680-08-5P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-2-[[4-[[(methylsulfonyl)amino]methyl]phenyl]amino]-N-methylacetamide 851680-15-4P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-2-[[3-[[(methylsulfonyl)amino]methyl]phenyl]amino]-N-methylacetamide 851680-16-5P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-2-[[2-[[(methylsulfonyl)amino]methyl]phenyl]amino]-N-methylacetamide 851680-17-6P, 2-(3,4-Dichlorophenylamino)-N-[2-((3S)-3-hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide

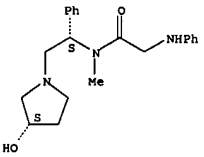
L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
851680-19-8P, 2-(4-Trifluoromethylphenylamino)-N-[2-((3S)-3-hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide 851680-20-1P, 2-[(2,4-Dichlorophenyl)(methylsulfonyl)amino]-N-[2-((3S)-3-hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide 851680-21-2P, 2-(4-Nitrophenylamino)-N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide 851680-22-3P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-2-[[4-[(methylsulfonyl)amino]phenyl]amino]-N-methylacetamide 851680-26-7P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-2-[[4-[(propylsulfonyl)amino]phenyl]amino]-N-methylacetamide 851680-28-9P, N-[(1S)-1-((3S)-3-Hydroxypyrrolidin-1-ylmethyl)-2-methylpropyl]-N-methyl-2-[[4-[(propan-1-ylsulfonyl)amino]phenyl]amino]acetamide 851680-29-0P, Propane-1-sulfonic acid N-[4-[[2-[(2S)-2-((3S)-3-hydroxypyrrolidin-1-ylmethyl)piperidin-1-yl]-2-oxoethyl]amino]phenyl]amide 851680-30-3P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-N'-phenylmalonamide 851680-34-7P, N-[4-[[(Methylsulfonyl)amino]methyl]phenyl]-N'-[2-((3S)-3-hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N'-methylmalonamide 851680-38-1P, N-[4-[[(Ethylsulfonyl)amino]methyl]phenyl]-N'-[2-((3S)-3-hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N'-methylmalonamide 851680-40-5P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N'-[4-[(methylsulfonyl)amino]phenyl]-N-methylmalonamide 851680-43-8P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-N'-[2-[(pyrrolidin-1-yl)sulfonyl]phenyl]malonamide 851680-46-1P, N-Benzyl-N'-[2-((3S)-3-hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N'-methylmalonamide 851680-47-2P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-N'-(thiazol-2-yl)malonamide 851680-48-3P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-N'-pyridin-3-ylmalonamide 851680-51-8P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-N'-phenylsuccinamide 851680-52-9P, N-[(1S)-1-((3S)-3-Hydroxypyrrolidin-1-ylmethyl)-2-methylpropyl]-N-methyl-N'-phenylsuccinamide 851680-53-0P, 4-[(2S)-2-((3S)-3-Hydroxypyrrolidin-1-ylmethyl)piperidin-1-yl]-4-oxo-N-phenylbutyramide 851680-54-1P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-N'-(thiazol-2-yl)succinamide 851680-55-2P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-N'-pyridin-3-ylsuccinamide 851680-57-4P, N-[2-((3S)-3-Hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methyl-2-(3-phenylureido)acetamide 851680-58-5P, N-[(1S)-1-((3S)-3-Hydroxypyrrolidin-1-ylmethyl)-2-methylpropyl]-N-methyl-2-(3-phenylureido)acetamide 851680-59-6P 851680-60-9P,

2-[(4-Aminomethylphenyl)amino]-N-[2-((3S)-3-hydroxypyrrolidin-1-yl)-(1S)-1-phenylethyl]-N-methylacetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of N-aminoalkyl amides as agonists of κ opioid receptor useful against gastrointestinal disorders, pain, and pruritus)

RN 851679-94-2 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-(phenylamino)- (9CI) (CA INDEX NAME)

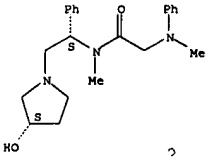
Absolute stereochemistry.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



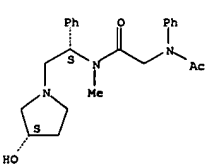
RN 851679-95-3 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-(methylphenylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851679-96-4 CAPLUS
CN Acetamide, 2-(acetylphenylamino)-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

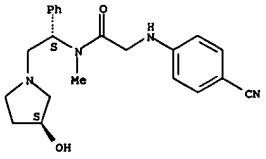
Absolute stereochemistry.



RN 851679-98-6 CAPLUS
CN Acetamide, 2-[(4-cyanophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

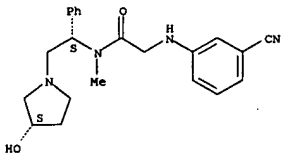
Absolute stereochemistry.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



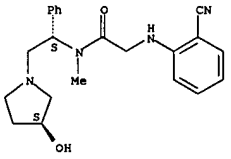
RN 851679-99-7 CAPLUS
CN Acetamide, 2-[(3-cyanophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851680-00-7 CAPLUS
CN Acetamide, 2-[(2-cyanophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

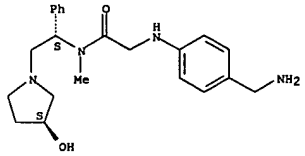
Absolute stereochemistry.



RN 851680-01-8 CAPLUS
CN Acetamide, 2-[[4-(aminomethyl)phenyl]amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
NAME)

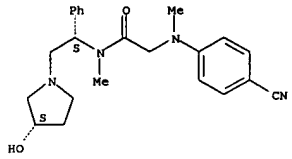
Absolute stereochemistry.



● HCl

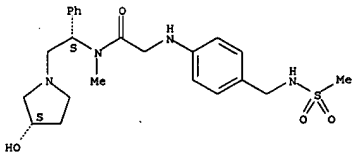
RN 851680-03-0 CAPLUS
CN Acetamide, 2-[(4-cyanophenyl)methylamino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



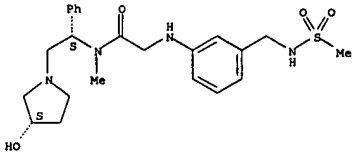
RN 851680-08-5 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-[[(methylsulfonyl)amino]methyl]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



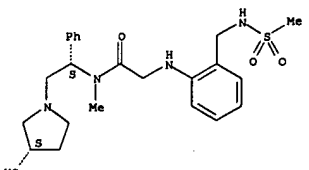
RN 851680-15-4 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[3-[[(methylsulfonyl)amino]methyl]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



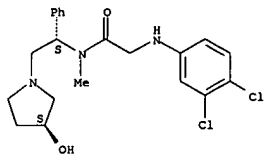
RN 851680-16-5 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[2-[[(methylsulfonyl)amino]methyl]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



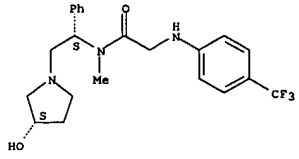
RN 851680-17-6 CAPLUS
CN Acetamide, 2-[(3,4-dichlorophenyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



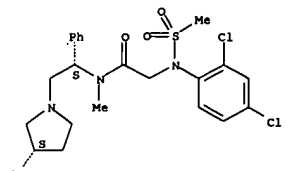
RN 851680-19-8 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-(trifluoromethyl)phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



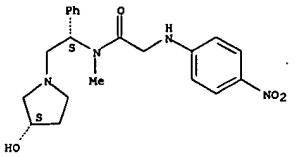
RN 851680-20-1 CAPLUS
CN Acetamide, 2-[(2,4-dichlorophenyl)(methylsulfonyl)amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



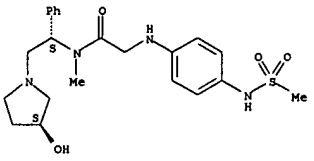
RN 851680-21-2 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[(4-nitrophenyl)amino]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



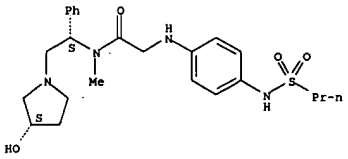
RN 851680-22-3 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-[(methylsulfonyl)amino]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



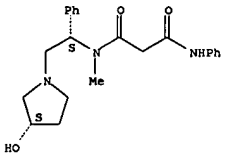
RN 851680-26-7 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[4-[(propylsulfonyl)amino]phenyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



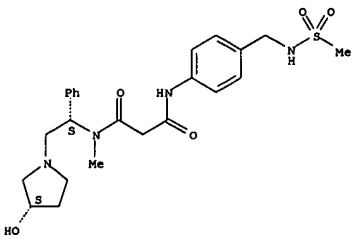
RN 851680-28-9 CAPLUS
CN Acetamide, N-[(1S)-1-[[(3S)-3-hydroxy-1-pyrrolidinyl]methyl]-2-methylpropyl]-N-methyl-2-[[4-[(propylsulfonyl)amino]phenyl]amino]- (9CI)

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 851680-34-7 CAPLUS
CN Propanediamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-[4-[[(methylsulfonyl)amino]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

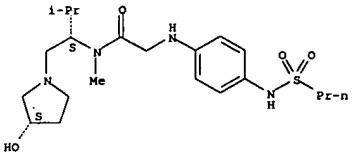


RN 851680-38-1 CAPLUS
CN Propanediamide, N'-[4-[[(ethylsulfonyl)amino]methyl]phenyl]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

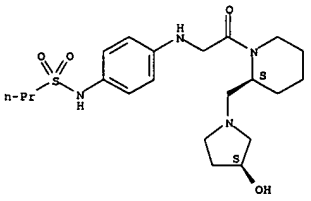
L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



RN 851680-29-0 CAPLUS
CN Piperidine, 2-[[(3S)-3-hydroxy-1-pyrrolidinyl]methyl]-1-[[[4-[(propylsulfonyl)amino]phenyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

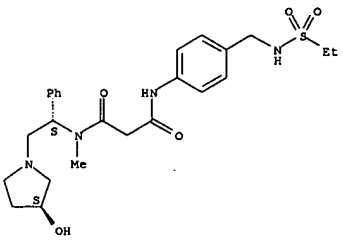
Absolute stereochemistry.



RN 851680-30-3 CAPLUS
CN Propanediamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-phenyl- (9CI) (CA INDEX NAME)

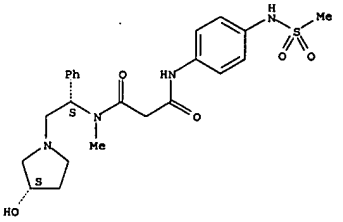
Absolute stereochemistry.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 851680-40-5 CAPLUS
CN Propanediamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-[4-[(methylsulfonyl)amino]phenyl]- (9CI) (CA INDEX NAME)

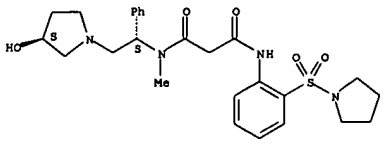
Absolute stereochemistry.



RN 851680-43-8 CAPLUS
CN Propanediamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-[2-(1-pyrrolidinylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

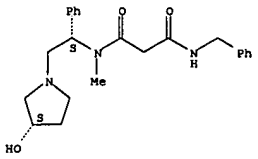
Absolute stereochemistry.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



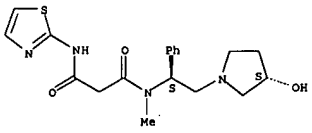
RN 851680-46-1 CAPLUS
CN Propanediamide,
N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851680-47-2 CAPLUS
CN Propanediamide,
N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-2-thiazolyl- (9CI) (CA INDEX NAME)

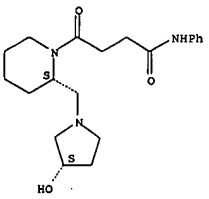
Absolute stereochemistry.



RN 851680-48-3 CAPLUS
CN Propanediamide,
N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-3-pyridinyl- (9CI) (CA INDEX NAME)

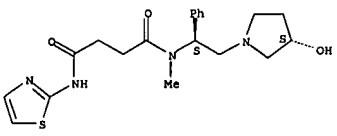
L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



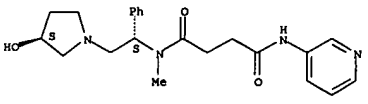
RN 851680-54-1 CAPLUS
CN Butanediamide,
N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-2-thiazolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851680-55-2 CAPLUS
CN Butanediamide,
N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-3-pyridinyl- (9CI) (CA INDEX NAME)

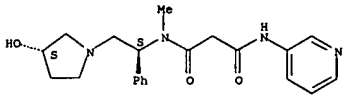
Absolute stereochemistry.



RN 851680-57-4 CAPLUS
CN Acetamide, N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-2-[[(phenylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

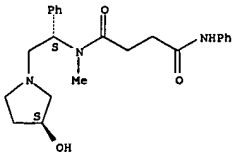
Absolute stereochemistry.

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



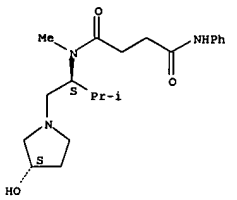
RN 851680-51-8 CAPLUS
CN Butanediamide,
N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl-N'-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



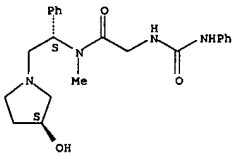
RN 851680-52-9 CAPLUS
CN Butanediamide, N-[(1S)-1-[[(3S)-3-hydroxy-1-pyrrolidinyl]methyl]-2-methylpropyl]-N-methyl-N'-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



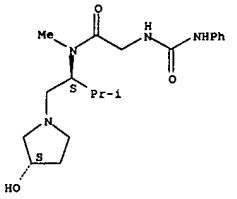
RN 851680-53-0 CAPLUS
CN 1-Piperidinebutanamide, 2-[[(3S)-3-hydroxy-1-pyrrolidinyl]methyl]-γ-oxo-N-phenyl-, (2S)- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



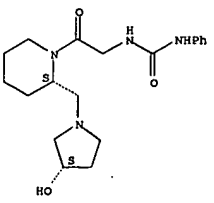
RN 851680-58-5 CAPLUS
CN Acetamide, N-[(1S)-1-[[(3S)-3-hydroxy-1-pyrrolidinyl]methyl]-2-methylpropyl]-N-methyl-2-[[(phenylamino)carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 851680-59-6 CAPLUS
CN Piperidine, 2-[[(3S)-3-hydroxy-1-pyrrolidinyl]methyl]-1-[[[(phenylamino)carbonyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

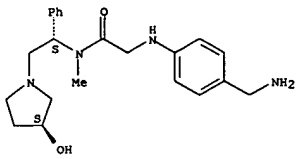
Absolute stereochemistry.



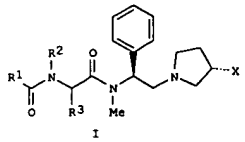
RN 851680-60-9 CAPLUS

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Acetamide, 2-[[4-(aminomethyl)phenyl]amino]-N-[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:130273 CAPLUS
DN 142:374089
TI Amino acid conjugates as κ opioid receptor agonists
AU Kumar, Virendra; Guo, Deqi; Daubert, Jeffrey D.; Cassel, Joel A.; DeHaven, Robert N.; Mansson, Erik; DeHaven-Hudkins, Diane L.; Maycock, Alan L.
CS Adolor Corporation, Exton, PA, 19341, USA
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(5), 1279-1282
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 142:374089
GI

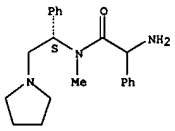


I

AB A novel series of kappa (κ) opioid receptor agonists were synthesized by incorporating the key structural features of known κ opioid agonists while replacing the aryl acetamide portion with substituted amino acid conjugates. Compds. I (R1 = Ph, 3,4-Cl2C6H3 or 1-oxido-2,1,3-benzoxadiazol-6-yl, R2, R3, X = H; R1 = 3,4-Cl2C6H3 or 4-MeOC6H4, R2, R3 = H, X = OH) possessed potent affinities for the κ opioid receptor (Ki = 6.7, 3.6, 4.6, 0.83, 2 nM, resp.) in vitro with reasonable selectivity over other opioid receptors.
IT 849517-36-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid conjugates as κ opioid receptor agonists)
RN 849517-36-8 CAPLUS
CN Benzeneacetamide, α-amino-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

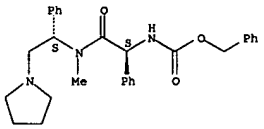
Absolute stereochemistry.

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



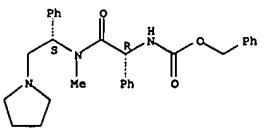
IT 849517-37-9P 849517-38-0P 849517-39-1P
849517-40-4P 849517-41-5P 849517-42-6P
849517-43-7P 849517-44-8P 849517-45-9P
849517-46-0P 849517-47-1P 849517-48-2P
849517-49-3P 849517-50-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of amino acid conjugates as κ opioid receptor agonists)
RN 849517-37-9 CAPLUS
CN Carbamic acid, [(1S)-2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxo-1-phenylethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849517-38-0 CAPLUS
CN Carbamic acid, [(1R)-2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxo-1-phenylethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

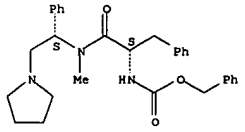
Absolute stereochemistry.



RN 849517-39-1 CAPLUS
CN Carbamic acid, [(1S)-2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

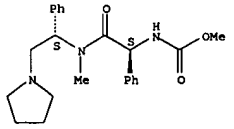
L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



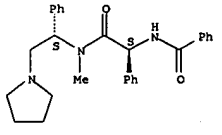
RN 849517-40-4 CAPLUS
CN Carbamic acid, [(1S)-2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxo-1-phenylethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849517-41-5 CAPLUS
CN Benzeneacetamide, α-(benzoylamino)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]-, (αS)- (9CI) (CA INDEX NAME)

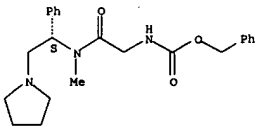
Absolute stereochemistry.



RN 849517-42-6 CAPLUS
CN Carbamic acid, [2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxoethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

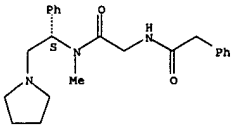
Absolute stereochemistry.

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



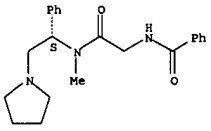
RN 849517-43-7 CAPLUS
CN Benzeneacetamide, N-[2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



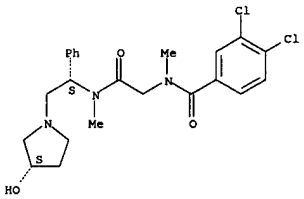
RN 849517-44-8 CAPLUS
CN Benzamide, N-[2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



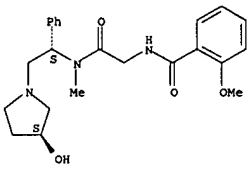
RN 849517-45-9 CAPLUS
CN Benzamide, 3,4-dichloro-N-[2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



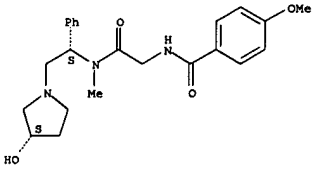
RN 849517-49-3 CAPLUS
CN Benzamide, N-[2-[[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]methylamino]-2-oxoethyl]-2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



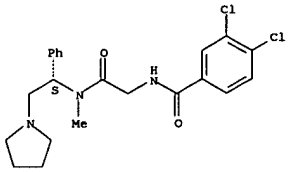
RN 849517-50-6 CAPLUS
CN Benzamide, N-[2-[[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]methylamino]-2-oxoethyl]-4-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



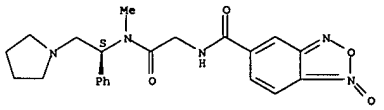
IT 849517-51-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



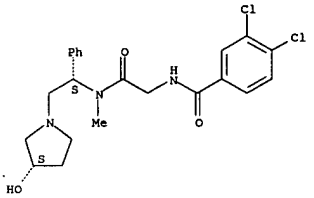
RN 849517-46-0 CAPLUS
CN 2,1,3-Benzoxadiazole-5-carboxamide, N-[2-[methyl[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]amino]-2-oxoethyl]-, 1-oxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 849517-47-1 CAPLUS
CN Benzamide, 3,4-dichloro-N-[2-[[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]methylamino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

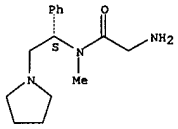


RN 849517-48-2 CAPLUS
CN Benzamide, 3,4-dichloro-N-[2-[[(1S)-2-[(3S)-3-hydroxy-1-pyrrolidinyl]-1-phenylethyl]methylamino]-2-oxoethyl]-N-methyl- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(Reactant or reagent)
(prepn. of amino acid conjugates as κ opioid receptor agonists)

RN 849517-51-7 CAPLUS
CN Acetamide, 2-amino-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



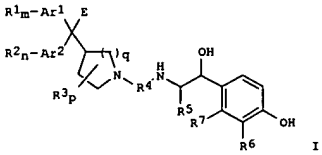
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:872779 CAPLUS
DN 141:350030
TI Preparation of (diphenyl)(pyrrolidinyl)methyl amides as β2 adrenergic receptor agonist and muscarinic receptor antagonist
IN Mammen, Mathai; Hughes, Adam
PA Theravance, Inc., USA
SO PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

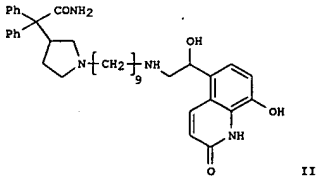
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004089892 | A2 | 20041021 | WO 2004-US9825 | 20040331 |
| | WO 2004089892 | A3 | 20041209 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1615881 | A2 | 20060118 | EP 2004-758642 | 20040331 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| PRAI | US 2003-459291P | P | 20030401 | | |
| | WO 2004-US9825 | W | 20040331 | | |

OS MARPAT 141:350030
GI

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



I



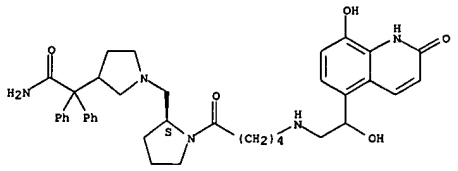
II

AB Title compds. represented by the formula I [wherein Ar1, Ar2 = independently Ph, (cyclo)alkyl, (un)substituted heteroaryl, heterocyclyl; m = 0-3; n = 0-3; R1-R3 = independently (cyclo)alkyl, alkenyl, alkynyl, cyano, etc.; E = CN, OH, carbonylamino, carboxylate; p = 0-4; R4 = a divalent; R5 = H or alkyl; R6 = carbamoyl or alkoxyalkyl; R7 = H or R6R7 = (un)substituted (hetero)cyclyl; q = 1-2; and pharmaceutically acceptable salts, solvates or stereoisomers thereof] were prepared as β2 adrenergic receptor agonist and muscarinic receptor antagonist. For example, II was given in a multi-step synthesis starting from the reaction of (S)-1-benzyl-3-pyrrolidinol with p-toluenesulfonyl chloride. II was tested for radioligand binding at human β1, β2 and β3 adrenergic receptors with a ration of Ki(β1)/Ki(β2) greater than 8, and with Ki values of less than 50 nM at human muscarinic receptors, etc. Thus, I and their pharmaceutical compns. are useful as β2 adrenergic receptor agonist and muscarinic receptor antagonist for the treatment of pulmonary disorders, such as chronic obstructive pulmonary disease and asthma.

IT 777064-44-5P 777065-88-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (diphenyl)(pyrrolidinyl)methyl amides as β2 adrenergic receptor agonist and muscarinic receptor antagonist)

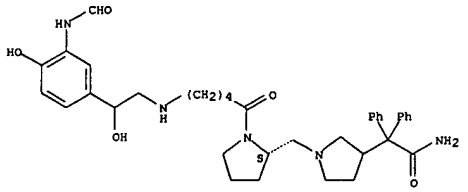
RN 777064-44-5 CAPLUS
CN 3-Pyrrolidineacetamide, 1-[[(2S)-1-[5-[[2-(1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl)-2-hydroxyethyl]amino]-1-oxopentyl]-2-pyrrolidinyl]methyl]-α,α-diphenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 777065-88-0 CAPLUS
CN 3-Pyrrolidineacetamide, 1-[[(2S)-1-[5-[[2-[3-(formylamino)-4-hydroxyphenyl]-2-hydroxyethyl]amino]-1-oxopentyl]-2-pyrrolidinyl]methyl]-α,α-diphenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:703125 CAPLUS
DN 141:225161
TI Preparation of biphenyl derivatives as β2-adrenergic agonists and muscarinic antagonists for pulmonary disorders.
IN Mammen, Mathai; Dunham, Sarah; Hughes, Adam; Lee, Tae Weon; Husfeld, Craig; Stangeland, Eric
PA USA
SO U.S. Pat. Appl. Publ., 85 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004167167 | A1 | 20040826 | US 2004-779157 | 20040213 |
| | AU 2004213411 | A1 | 20040902 | AU 2004-213411 | 20040213 |
| | CA 2515777 | AA | 20040902 | CA 2004-2515777 | 20040213 |
| | WO 2004074276 | A1 | 20040902 | WO 2004-US4224 | 20040213 |
| | WO 2004074276 | B1 | 20041007 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | WO 2004074812 | A2 | 20040902 | WO 2004-US4273 | 20040213 |
| | WO 2004074812 | A3 | 20041104 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | WO 2004074246 | A2 | 20040902 | WO 2004-US4449 | 20040213 |
| | WO 2004074246 | A3 | 20041118 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2004209915 | A1 | 20041021 | US 2004-778290 | 20040213 |
| | US 2004209860 | A1 | 20041021 | US 2004-778649 | 20040213 |
| | EP 1592685 | A1 | 20051109 | EP 2004-711137 | 20040213 |
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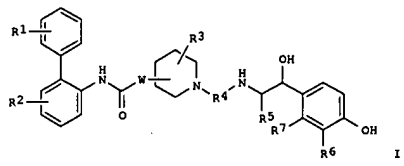
| | EP 1594860 | A2 | 20051116 | EP 2004-711117 | 20040213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | EP 1615889 | A2 | 20060118 | EP 2004-711253 | 20040213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2004007508 | A | 20060214 | BR 2004-7508 | 20040213 |
| | CN 1759108 | A | 20060412 | CN 2004-80006528 | 20040213 |

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

| | | | | | |
|---|---|---|---|---|---|
| | NO 2005004206 | A | 20051019 | NO 2005-4206 | 20050909 |
| PRAI | US 2003-447843P | P | 20030214 | | |
| | US 2003-467035P | P | 20030501 | | |
| | WO 2004-US4224 | W | 20040213 | | |
| | WO 2004-US4273 | W | 20040213 | | |
| | WO 2004-US4449 | W | 20040213 | | |

OS MARPAT 141:225161
GI



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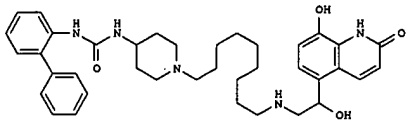


II

AB Title compds. I [R1 (taken 0-3 times) = alk(en/yn)yl, cycloalkyl, etc.; R2 (taken 0-3 times) = alk(en/yn)yl, cycloalkyl, CN, etc.; W = O, substituted N; R3 (taken 0-4 times) = alk(en/yn)yl, cycloalkyl, etc.; R4 = divalent group; R5 = H, alkyl; R6 = amino, alkoxy, etc.; R7 = H, etc.] are prepared For instance, N-[1,1'-Biphenyl-2-yl]-N'-[1-(9-aminononyl)piperidin-4-yl]urea (preparation given) is combined with 8-Benzyloxy-5-(2,2-dihydroxyacetyl)-1H-quinolin-2-one (CH2Cl2, NaHB(OAc)3) and the product reduced (MeOH, H2-Pd/C) to give II. Selected example compds. have Ki < 10 nM for the β2 and muscarinic receptor. I are useful in the treatment of pulmonary disorders, such as chronic obstructive pulmonary disease and asthma.

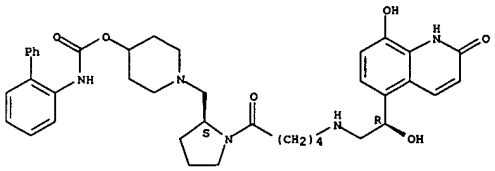
IT 743461-85-0P, Biphenyl-2-ylcarbamic acid 1-[[(2S)-1-[5-[[(R)-2-

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

hydroxy-2-(8-hydroxy-2-oxo-1,2-dihydroquinolin-5-yl)ethyl]amino]pentanoyl]pyrrolidin-2-yl]methyl]piperidin-4-yl ester RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenyl derivs. as β2-adrenergic agonists and muscarinic antagonists for pulmonary disorders)

RN 743461-85-0 CAPLUS
CN Carbamic acid, [1,1'-biphenyl]-2-yl-, 1-[[(2S)-1-[5-[[(2R)-2-(1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl)-2-hydroxyethyl]amino]-1-oxopentyl]-2-pyrrolidinyl]methyl]-4-piperidinyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



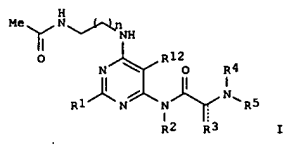
L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:511098 CAPLUS
DN 139:85366
TI Preparation of N-(pyrimidin-4-yl)acetamides as A2b adenosine receptor selective antagonists
IN Castelhano, Arlindo; McKibben, Bryan; Steinig, Arno; Collington, Eric William
PA OSI Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003053366 | A2 | 20030703 | WO 2002-US41273 | 20021220 |
| | WO 2003053366 | A3 | 20040129 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2471059 | AA | 20030703 | CA 2002-2471059 | 20021220 |
| | AU 2002366811 | A1 | 20030709 | AU 2002-366811 | 20021220 |
| | US 2003162764 | A1 | 20030828 | US 2002-326204 | 20021220 |
| | US 6916804 | B2 | 20050712 | | |
| | BR 2002015202 | A | 20041013 | BR 2002-15202 | 20021220 |
| | EP 1465631 | A2 | 20041013 | EP 2002-805676 | 20021220 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | CN 1620294 | A | 20050525 | CN 2002-828270 | 20021220 |
| | JP 2005517659 | T2 | 20050616 | JP 2003-554126 | 20021220 |
| | US 2005119271 | A1 | 20050602 | US 2004-992239 | 20041118 |
| PRAI | US 2001-342595P | P | 20011220 | | |
| | US 2002-326204 | A1 | 20021220 | | |
| | WO 2002-US41273 | W | 20021220 | | |

OS MARPAT 139:85366
GI

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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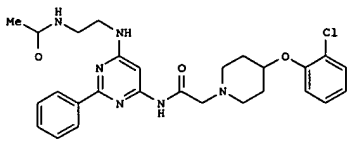
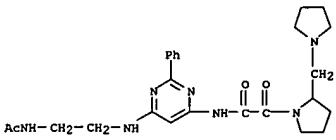


II

AB Title compds. I [wherein R1 = (un)substituted Ph, heterocyclyl, or heteroaryl; R2 and R3 = independently H or (un)substituted (cyclo)alkyl, alkanoyl, alkoxy(carbonyl), alkenyl, monocyclic or bicyclic aryl, heteroaryl, or heterocyclyl; or R2 and R3 are joined to form a heterocyclic ring; wherein the dashed line = a double bond which may be present or absent, and when present R3 = O; R4 and R5 = independently (un)substituted (cyclo)alkyl, alkanoyl, alkoxy(carbonyl), alkenyl, monocyclic or bicyclic aryl, heteroaryl, or heterocyclyl; or NR4R5 = (un)substituted monocyclic or bicyclyl, heterocyclyl, or heteroaryl; R12 = H, alkyl, halo, or cyano; n = 0-4; or enantiomers, tautomers, or pharmaceutically acceptable salts thereof] were prepared as A2b adenosine receptor antagonists. For example, cycloaddn. of benzamidine•HCl and di-Et malonate using DBU in DMF gave 2-phenylpyrimidine-4,6-diol (73%). Chlorination (95%), amination (93%), substitution with N-(2-aminoethyl)acetamide (57%), and amidation with chloroacetyl chloride (91%) provided N-[6-(2-acetylaminoethylamino)-2-phenylpyrimidin-4-yl]-2-chloroacetamide. Coupling of the chloroacetamide with 4-(2-chlorophenoxy)piperidine in the presence of NaI and DIPEA in 3:1 acetonitrile:THF afforded II (86%). Compds. of the invention showed greater than tenfold selectivity for the human A2b adenosine receptor (Ki values <100 nM) over the A1, A2a, and A3 receptors in radioligand binding assays. Thus, I and pharmaceutical compns. comprising I are useful for the treatment of diseases associated with the A2b adenosine receptor, such as asthma, diabetes, or proliferating tumors associated with mast cell degranulation (no data).

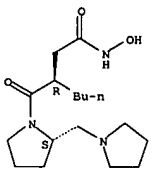
IT 552870-53-8P, N-[6-[[2-(Acetylamino)ethyl]amino]-2-phenylpyrimidin-4-yl]-2-oxo-2-[2-[(pyrrolidin-1-yl)methyl]pyrrolidin-1-yl]acetamide RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(A2b antagonist; preparation of N-(pyrimidinyl)acetamides as A2b adenosine receptor selective antagonists for treatment of asthma, diabetes,

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
tumors, and other A2b assocd. diseases)
RN 552870-53-8 CAPLUS
CN 1-Pyrrolidineacetamide, N-[6-[[2-(acetylamino)ethyl]amino]-2-phenyl-4-pyrimidinyl]-α-oxo-2-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(prepn. of novel succinate compds. as peptide deformylase inhibitors)
RN 345344-97-0 CAPLUS
CN 1-Pyrrolidinebutanamide, β-butyl-N-hydroxy-γ-oxo-2-(1-pyrrolidinylmethyl)-, (βR,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

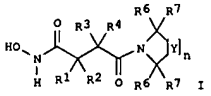


RE.CNT 208 THERE ARE 208 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:638332 CAPLUS
DN 137:169789
TI Preparation of novel succinate compounds as peptide deformylase inhibitors
IN Patel, Dinesh; Jacobs, Jeffrey W.; Jain, Rakesh; Ni, Zhi-jie; Yuan, Zhengyu
PA Vicuron Pharmaceuticals Inc., USA
SO U.S. Pat. Appl. Publ., 84 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2002115863 | A1 | 20020822 | US 2000-738859 | 20001213 |
| US 6797820 | B2 | 20040928 | | |
| PRAI US 2000-738859 | | 20001213 | | |

OS MARPAT 137:169789
GI



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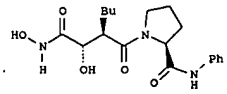


II

AB Title hydroxamates I [R1,R3 = H, halo, OH, etc.; R2, R4 = H, alkyl, heteroalkyl, etc.; n = 1-5; zero or one of Y = O, NR11 (R11 = alkyl, heteroalkyl, alkenyl, etc.), S, and all remaining Y = CR6R7; R6, R7 = H, OH, NH2, etc.] which inhibit peptide deformylase (PDF), an enzyme present in prokaryotes, and useful as antimicrobials and antibiotics, were prepared and formulated. E.g., a multi-step synthesis of II was given. MIC for various compds. I against H. influenza and S. aureus was approx. 64 μg/mL or less. The compds. I display selective inhibition of peptidyl deformylase vs. other metalloproteinases such as matrix metalloproteinases (MMPs).
IT 345344-97-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

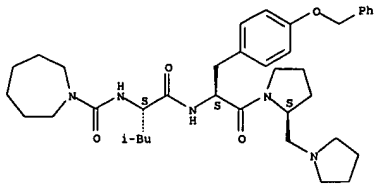
L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:552324 CAPLUS
DN 137:109488
TI Preparation of peptidyl calcium channel blockers
IN Booth, Richard John; Brogley, Louis; Cody, Wayne Livingston; Connor, David Thomas; Hamilton, Harriet Wall; He, John Xiaoqiang; Hu, Lain-Yen; Lescosky, Leonard Joseph; Malone, Thomas Charles; Nadasdi, Laszlo; Rafferty, Michael Francis; Roth, Bruce David; Silva, Diego F.; Song, Yuntao; Szoke, Balazs G.; Urge, Laszlo
PA Warner-Lambert Company, USA; Neurex Corporation
SO U.S., 86 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 6423689 | B1 | 20020723 | US 1998-212785 | 19981216 |
| PRAI US 1997-68485P | P | 19971222 | | |

OS MARPAT 137:109488
AB Peptides R5CONHCR1R7CONHCR2(CH2-p-C6H4-Y-R4)COR3 [R1 = alkyl, benzyl, H, indolylmethyl, Q-(CH2)n (Q = alkylthio, substituted Ph, cycloalkyl, heteroaryl; n = 0-5); R2 = H, alkyl; R3 = alkoxy, Ph(CH2)nO, NH2, alkylamino, cycloalkyl, etc.; R4 = Q(CH2)n, where Q = (un)substituted Ph, NH2, dialkylamino, pyridyl, etc.; R5 = N(CH2)m (m = 2-7); R7 = H, alkyl; Y = O, NR4, NH, absent, CH:CH, C.tplbond.C] or their pharmaceutically acceptable salts, esters, amides, and prodrugs were prepared as calcium channel blockers. Pharmaceutical compns. containing these compds. can be used to treat stroke, cerebral ischemia, head trauma, or epilepsy. Thus, {S-(R*,R*)}-2-[2-[(azepane-1-carbonyl)amino]-4-methylpentanoylamino]-3-(4-benzyloxy-phenyl)propionic acid tert-Bu ester was prepared via amidation reaction and showed IC50 = 0.35 μM for inhibition of calcium flux in IMR-32 cells and protected 5/5 mice from tonic convulsions at 30 mg/kg at 15 min posttreatment time. The syntheses of 271 compds. of the invention are described in the examples and > 200 addnl. compds. are given in the claims.
IT 443691-67-6P 443693-06-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidyl calcium channel blockers)
RN 443691-67-6 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-3-methyl-1-[[[(1S)-2-oxo-1-[[4-(phenylmethoxy)phenyl]methyl]-2-[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]ethyl]amino]carbonyl]butyl]- (9CI) (CA INDEX NAME)

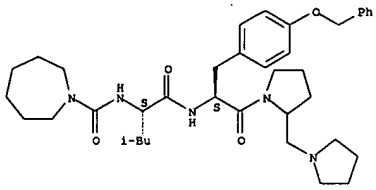
Absolute stereochemistry.

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 443693-06-9 CAPLUS
CN 1H-Azepine-1-carboxamide, hexahydro-N-[(1S)-3-methyl-1-[[[(1S)-2-oxo-1-[[4-(phenylmethoxy)phenyl]methyl]-2-[2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]ethyl]amino]carbonyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

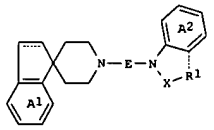


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:256237 CAPLUS
DN 136:294733
TI Preparation of spiro compounds as nociceptin receptor binders
IN Arai, Toshimitsu; Nishikimi, Yuji; Imamura, Shinichi; Kamiyama, Keiji; Kobayashi, Makoto
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002026714 | A1 | 20020404 | WO 2001-JP8281 | 20010925 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2001088110 | A5 | 20020408 | AU 2001-88110 | 20010925 |
| | JP 2002173485 | A2 | 20020621 | JP 2001-291794 | 20010925 |
| PRAI | JP 2000-293876 | A | 20000927 | | |
| | WO 2001-JP8281 | W | 20010925 | | |

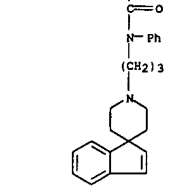
OS MARPAT 136:294733
GI



I

AB The title compds. I [A1 and A2 are each an optionally substituted benzene ring; E is a divalent chain hydrocarbon group which may be substituted; X is CO or the like; R1 is an optionally substituted hydrocarbon group or the like, or alternatively R1 may be bonded to a ring-constituting carbon atom of A2 to form a fused ring; and the dotted line represents a single or double bond; a proviso is given] are prepared Processes for preparing I are claimed. In an in vitro test for affinity for the nociceptin receptor, N-[3-(1H-indene-1-spiro-4'-piperidin-1'-yl)propyl]-1-methyl-5-oxo-N-phenyl-3-pyrrolidinecarboxamide fumarate at 1 μM gave 95% binding inhibition.

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Formulations are given.
IT 407632-52-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of spiro compds. as nociceptin receptor binders)
RN 407632-52-4 CAPLUS
CN 1-Pyrrolidinepentanamide, δ-oxo-N-phenyl-2-(1-pyrrolidinylmethyl)-N-(3-spiro[1H-indene-1,4'-piperidin]-1'-ylpropyl)- (9CI) (CA INDEX NAME)

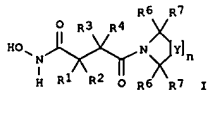


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

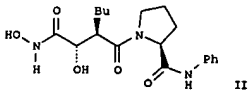
L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:453007 CAPLUS
DN 135:61546
TI Preparation of novel succinate compounds as peptide deformylase inhibitors
IN Jain, Rakesh; Ni, Zhi-jie; Patel, Dinesh V.; Yuan, Zhengyu
PA Versicor, Inc., USA; Jacobs, Jeffrey, W.
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001044179 | A1 | 20010621 | WO 2000-US34128 | 20001213 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2393825 | AA | 20010621 | CA 2000-2393825 | 20001213 |
| | EP 1237862 | A1 | 20020911 | EP 2000-986446 | 20001213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2003534239 | T2 | 20031118 | JP 2001-545267 | 20001213 |
| PRAI | US 1999-466402 | A1 | 19991217 | | |
| | WO 2000-US34128 | W | 20001213 | | |

OS MARPAT 135:61546
GI



I

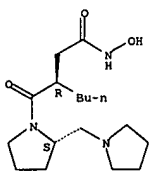


II

AB The title hydroxamates [I; R1 = H, halo, OH, etc.; R2 = H, alkyl, heteroalkyl, etc.; R3 = H, halo, OH, etc.; R4 = H, alkyl, heteroalkyl, etc.; n = 1-5; zero or one of Y = O, NR11 (wherein R11 = alkyl, heteroalkyl, alkenyl, etc.), S, and all remaining Y = CR6R7; R6, R7 = H, OH, NH2, etc.] which inhibit peptide deformylase (PDF), an enzyme present in prokaryotes, and useful as antimicrobials and antibiotics, were prepared

L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
and formulated. E.g., a multi-step synthesis of II was given. MIC for various compds. I against H. influenza and S. aureus was approx. 64 μg/mL or less. The compds. I display selective inhibition of peptidyl deformylase vs. other metalloproteinases such as matrix metalloproteinases (MMPs).
IT 345344-97-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel succinate compds. as peptide deformylase inhibitors)
RN 345344-97-0 CAPLUS
CN 1-Pyrrolidinebutanamide, β-butyl-N-hydroxy-γ-oxo-2-(1-pyrrolidinylmethyl)-, (βR,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

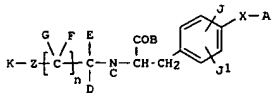


RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:380546 CAPLUS
DN 134:367194
TI Preparation of novel phenylalanine derivatives as α4-integrin inhibitors
IN Tanaka, Yasuhiro; Yoshimura, Toshihiko; Izawa, Hiroyuki; Ejima, Chieko; Kojima, Mitsuhiko; Atake, Yuko; Nakanishi, Eiji; Suzuki, Nobuyasu; Makino, Shingo; Suzuki, Manabu; Murata, Masahiro
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001036376 | A1 | 20010525 | WO 2000-JP8152 | 20001120 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001014165 | A5 | 20010530 | AU 2001-14165 | 20001120 |
| EP 1233013 | A1 | 20020821 | EP 2000-976347 | 20001120 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2003149083 | A1 | 20030807 | US 2002-150067 | 20020520 |
| US 6855706 | B2 | 20050215 | | |
| US 2005070485 | A1 | 20050331 | US 2004-986829 | 20041115 |
| PRAI JP 1999-328468 | A | 19991118 | | |
| JP 2000-197139 | A | 20000629 | | |
| WO 2000-JP8152 | W | 20001120 | | |
| US 2002-150067 | A1 | 20020520 | | |

OS MARPAT 134:367194
GI

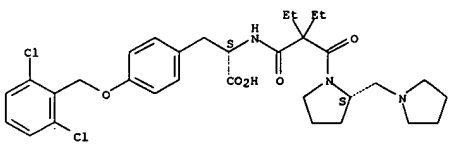


I

AB Phenylalanine derivs. represented by general formula (I) or pharmaceutically acceptable salts thereof [wherein X represents an interat. bond, O, OSO2, N-(un)substituted NH, NHCO, NHSO2, NHCONH, or NH(CS)NH, CO; Y and Z represent each CO, SO, or SO2; A represents a specific substituted Ph group or nitrogen-contg. heterocycle such as arom.-fused pyrimidinedione or pyrimidinone, 2,4- or 2,5-imidazolidinedione, or 5-imidazolone; C represents hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally contg. heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl; D and E represent each lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally contg. heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or D and E may be bonded to each other to form a ring optionally contg. 1 or 2 O, N, or S in the ring; F and G represent each hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally contg. heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or F and G may be bonded to each other to form a ring; n is from 0 to 2; K represents OR7, NR7R8, NHNR7R8, SR7, or R7; R7 and R8 represents H, lower alkyl, etc.; and J and J' represent each hydrogen, halogeno, lower alkyl, lower alkoxy, or NO2] are prepd. These derivs. and analogs thereof show an α4 integrin inhibitory activity and are usable as remedies for various diseases relating to α4 integrin, such as inflammatory diseases related to α4 integrin-dependent adhesion process, arthritis, inflammatory intestinal diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren syndrome, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, or transplant rejection. Thus, O-(2,6-dichlorobenzyl)-L-tyrosine bound to Wang resin was allowed to react with diethylmalonic acid, HOAt, 2-dimethylaminoisopropyl chloride hydrochloride (DIC), and N-methyl-2-pyrrolidinone (NMP) at room temp. for 16 h, washed with DMF five times, and condensed with pyrroline using HOAt, DIC, and NMP, followed by oxidn. with OsO4 in dioxane at room temp. for 16 and resin-cleavage in aq. CF3CO2H to give N-[2-[(cis-2,4-dihydroxypyrrolidin-1-yl)carbonyl]-2-ethylbutanoyl]-O-(2,6-dichlorobenzyl)-L-tyrosine (II). II and N-[2-[(pyrrolidin-1-yl)carbonyl]-2-ethylbutanoyl]-4-(2,6-dichlorobenzoylamino)-L-phenylalanine inhibited the binding of human recombinant VCAM-1 to human B lymphoma cell line expressing integrinα4β7 with IC50 of ≤0.02 μmol/L.
IT 340715-15-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel phenylalanine derivs. as α4-integrin inhibitors)
RN 340715-15-3 CAPLUS
CN L-Tyrosine, O-[(2,6-dichlorophenyl)methyl]-N-[2-ethyl-1-oxo-2-[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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                ROLAND E III"/AU OR "DOLLE ROLAND E JR"/AU OR "DOLLE ROLAND
                ELLWOOD"/AU OR "DOLLE ROLAND ELLWOOD III"/AU)
L6           27 SEA FILE=CAPLUS ABB=ON  PLU=ON  "CHU GUO HUA"/AU
L7           12 SEA FILE=CAPLUS ABB=ON  PLU=ON  "GU MINGHUA"/AU
L8          196 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 OR L6 OR L7
L9           31 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND OPIOID
L10           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 AND PYRROLID?

=> d 1-8 bib abs
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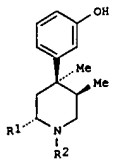
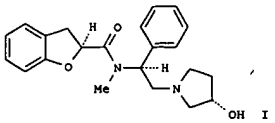
L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:16574 CAPLUS
DN 144:274106
TI Synthesis and structure-activity relationships of a new series of 2α-substituted trans-4,5-dimethyl-4-(3-hydroxyphenyl)piperidine as μ-selective opioid antagonists
AU Le Bourdonnec, Bertrand; Goodman, Allan J.; Michaut, Mathieu; Ye, Hai-Fen; Graczyk, Thomas M.; Belanger, Serge; DeHaven, Robert N.; Dolle, Roland E.
CS Department of Chemistry, Adolor Corporation, Exton, PA, 19341, USA
SO Bioorg. Med. Chem. Lett. (2006), 16(4), 864-868
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:274106
GI



I

AB Structure-activity relationships at the 2α-position of the piperidine ring of the trans-4,5-dimethyl-4-(3-hydroxyphenyl)piperidine μ- opioid antagonist series I [R1 = H, Me, Me2CH, H2NCH2CH2, Ph, PhCH2, etc., R2 = PhCH2CH2; R1 = n-Pr, R2 = H, Me, n-Bu, PhCH2, Ph(CH2)3, etc.] were investigated. This study showed that only small linear alkyl groups (Me, propyl) are tolerated at the 2α-position of the piperidine ring of this series.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

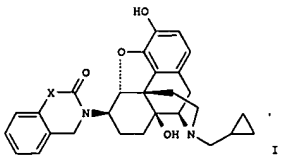
L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1144467 CAPLUS
DN 144:51411
TI Potent and highly selective kappa opioid receptor agonists incorporating chroman- and 2,3-dihydrobenzofuran-based constraints
AU Chu, Guo-Hua; Gu, Minghua; Cassel, Joel A.; Belanger, Serge; Graczyk, Thomas M.; DeHaven, Robert N.; Conway-James, Nathalie; Koblish, Mike; Little, Patrick J.; DeHaven-Hudkins, Diane L.; Dolle, Roland E.
CS Department of Chemistry, Adolor Corporation, Exton, PA, 19341, USA
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(23), 5114-5119
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
GI



I

AB Two chemical classes of kappa opioid receptor agonists, chroman-2-carboxamide derivs. and 2,3-dihydrobenzofuran-2-carboxamide derivs., e.g., I, were synthesized. These agents exhibited high and selective affinity for the kappa opioid receptor.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1056264 CAPLUS
DN 143:477783
TI Solid/solution-phase annulation reagents: Single-step synthesis of cyclic amine derivatives
AU Dolle, Roland E.; MacLeod, Calum; Martinez-Teipel, Blanca; Barker, William; Seida, Pamela R.; Herbertz, Torsten
CS Department of Chemistry, Adolor Corporation, Exton, PA, 19341, USA
SO Angewandte Chemie, International Edition (2005), 44(36), 5830-5833
CODEN: ACIEF5; ISSN: 1433-7851
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 143:477783
GI



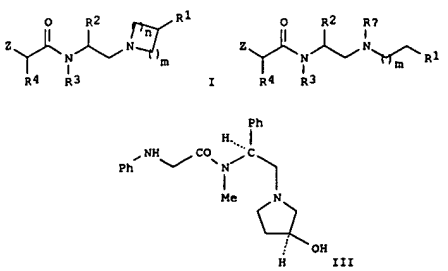
I

AB Iodo- or bromo-substituted propargyl esters undergo copper-catalyzed cycloaddns. with Merrifield resin-bound azide to yield resin-bound esters that are stable under ambient conditions; upon microwave irradiation with amines and a resin-bound carbonate, substitution of the halides followed by cyclization and resin cleavage provides lactams such as I (X = single bond, CH2) in 17-62% yields and in >90% purities after chromatog. purification
A wide variety of lactams containing 5- and 6-membered rings are prepared using the triazole-linked Merrifield resin-bound esters, allowing for facile introduction of diversity into combinatorial libraries; 7-membered ring can be prepared if the linker contains conformational constraints such as a benzene ring. A library of potential opioid receptor-binding compds. is prepared by this methodol. I (X = single bond), prepared from 6β-naltrexamine and triazole-linked Merrifield resin-bound 2-bromomethylbenzoate, binds to the μ- opioid receptor with a Ki value of 1.6 nM, while I (X = CH2) [prepared analogously from resin-bound 2-(bromomethyl)phenylacetate] binds to the same receptor with a Ki value of 56 nM. The electrostatic potential surfaces of some of the prepared compds. are determined by mol. mechanics calcns.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:431398 CAPLUS
DN 142:463595
TI Preparation of N-aminoalkyl amides as agonists of the κ opioid receptor useful against gastrointestinal disorders, pain, and pruritus
IN Dolle, Roland E.; Chu, Guo-Hua; Gu, Minghua
PA USA
SO U.S. Pat. Appl. Publ., 46 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2005107355 | A1 | 20050519 | US 2003-713746 | 20031114 |
| WO 2005049564 | A1 | 20050602 | WO 2004-US37955 | 20041112 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI US 2003-713746 | A | 20031114 | | |

OS MARPAT 142:463595
GI



I II



III

AB Amide derivs. (shown as I and II; variables defined below; e.g. N-[2-((S)-3-hydroxypyrrolidin-1-yl)-(S)-1-phenylethyl]-N-methyl-2-phenylaminoacetamide (shown as III)) are disclosed. Pharmaceutical compns. containing these compds., and methods for their use, inter alia, for treating and/or preventing gastrointestinal disorders, pain, and pruritus (no data) are also disclosed. Although the methods of preparation are not

L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
claimed, 36 example prepns. are included. For example, III was prepd. (45
%) by coupling of N-phenylglycine with
N-[2-((S)-3-hydroxypyrrolidin-1-yl)-
(S)-1-phenylethyl]-N-methylamine dihydrochloride. For I and II: R1 is H or OH; Ra is alkyl; R2 is alkyl, aryl, or aralkyl; R3 is alkyl, or R2 and R3 taken together with the atoms through which they are connected form a 4- to 8-membered heterocyclic ring; R4 is H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl, heteroaryl, or heteroarylalkyl; Z is -(CH2)oNR5R6 or -(CH2)oC(:O)NR7R8; R5 is H, alkyl, or aryl; R6 is aryl, alkaryl, -CO(NH)pR9, or -SO2R9, provided that at least one of R5 and R6 is
other than aryl; R7 is H or alkyl; R8 is alkyl, aryl, aralkyl, alkaryl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl; R9 is alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl, heteroaryl, or heteroarylalkyl; m is the integer 1, 2, or 3; n is the integer 1, 2, or 3;
o is the integer 0, 1, 2, or 3; p is the integer 0 or 1; and the quantity (m+n) is an integer 2-5. Compds. in all the examples showed κ receptor affinity (K1) <10 μM. For example, III had a Ki = 0.17 nM against the human κ receptor with >100+ selectivity vs. the human μ and δ receptors and was an agonist with an EC50 = 0.05 nM. It exhibited a % A = 96.2% at a dose of 300 μg, i.paw in the in vivo formalin-induced nociception assay. This compd. also blocked the action of HOAc-induced writhing when administered s.c. with an ED50 = 0.017 mg/kg.

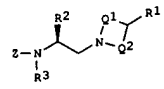
L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:220129 CAPLUS
DN 142:298013
TI Preparation of pyrrolidinylphenethyl benzoxepine-, tetrahydronaphthalene-, chroman-, and benzofurancarboxamides as κ-opioid agonists.
IN Dolle, Roland E.; Chu, Guo-Hua
PA Adolor Corporation, USA
SO U.S. Pat. Appl. Publ., 81 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2005054630 | A1 | 20050310 | US 2003-651197 | 20030828 |
| | US 7034051 | B2 | 20060425 | | |
| | WO 2005023799 | A1 | 20050317 | WO 2004-US27307 | 20040820 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-651197 A 20030828
OS MARPAT 142:298013
GI

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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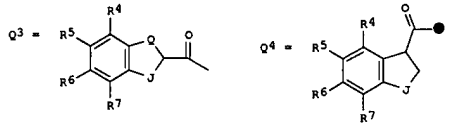
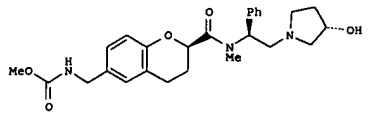






II

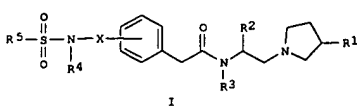
AB Title compds. [I; R1 = H, OH; R2 = alkyl, aralkyl, aryl; R3 = alkyl, aralkyl; Q1, Q2 = (CH2)1-2; Z = Q3, Q4; Q = O, CH2, NR8; J = (CH2)k, O(CH2)k-1, CH:CHCH2, CABCH2; k = 1-3; A = H, B = H, alkyl; AB = O, CH2; R4-R7 = H, alkyl, halo, aryl, heteroaryl, OH, NO2, cyano, CF3, CF2CF3, OCF3, etc.; R8 = H, alkyl, acyl], were prepared Thus, title compound (II)
(preparation outlined) blocked acetic acid-induced writhing with ED50 = 0.53
mg/kg s.c.
RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1080691 CAPLUS
DN 142:56168
TI Preparation of sulfonylamino pyrrolidinylethyl phenylacetamide derivatives and their opioid receptor binding affinity
IN Le Bourdonnec, Bertrand; Ajello, Christopher William; Dolle, Roland E.
PA Adolor Corporation, USA
SO U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004254156 | A1 | 20041216 | US 2003-458135 | 20030610 |
| | US 6992193 | B2 | 20060131 | | |
| | WO 2005004796 | A2 | 20050120 | WO 2004-US18367 | 20040609 |
| | WO 2005004796 | A3 | 20050428 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-458135 A 20030610
OS MARPAT 142:56168
GI



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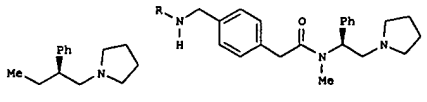

II III

AB The authors prepared the title compds. I [R1 = H, OH, R2 = alkyl, aryl, R3 =
H, alkyl, R2R3 = heterocyclyl,, R4 = H, alkyl, R5 = alkyl, aryl,

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
heterocycloalkyl, X = (CH2)n, n = 0, 1] and tested them for the ability to
inhibit the binding of non-selective opioid antagonist, [3H]diprenorphinc, to the cloned human μ, κ, and δ opioid receptors. To illustrate the prepn. method, 4-BrC6H4CH2CO2H was esterified to the Me ester, which was subsequently converted to the nitrile, reduced to the amine, and N-protected with Boc2O. This Boc-protected compd. was then hydrolyzed to the acid and coupled with (S)-pyrrolidinylamine II to give amide III (R = NHBoc) (IV). IV was then deprotected, N-acetylated, and then N-mesylated to give III (R = SO2Me). To summarize the activity, the compds. (1) bind with high affinity to κ opioid receptors; (2) display good opioid receptor selectivity of κ vs. μ and κ vs. δ; and (3) do not substantially inhibit cytochrome P 450 enzymic activity, in particular CYP2D6, CYP2C9 and CYP3A4.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:878146 CAPLUS
DN 141:366142
TI Preparation of lactams for use in pharmaceutical compositions as κ-opioid receptor agonists
IN Dolle, Roland E.; Tuthill, Paul Anson
PA Adolor Corporation, USA
SO U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004209857 | A1 | 20041021 | US 2003-414802 | 20030416 |
| | US 6852713 | B2 | 20050208 | | |
| | WO 2004093796 | A2 | 20041104 | WO 2004-US11831 | 20040416 |
| | WO 2004093796 | A3 | 20050909 | | |

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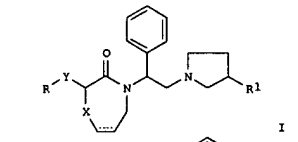
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-414802 A 20030416
OS MARPAT 141:366142
GI



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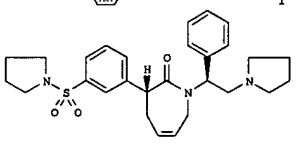
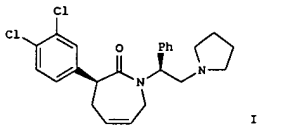


II

AB Lactam derivs., such as I [R = alkyl, aryl; R1 = H, OH; X = CH2, (CH2)2,

L10 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
OCH2; Y = bond, O], were prepd. for therapeutic use as κ-opioid receptor agonists which are useful for treatment of pruritic dermatosis, allergic dermatitis, atopy, contact dermatitis, psoriasis, eczema, opioid-induced pruritus, insect bites, cerebral edema and oxygen supply deficiency of the central nervous system and for inducing diuresis. Pharmaceutical compns. contg. the prepd. lactams and methods for their use were also disclosed. Thus, lactam II was prepd. via a multistep synthetic sequence which started from (S)-PhCH(NH2)CO2H, pyrrolidine and R2SO2-3-C6H4CH(CH2CH:CH2)CO2H (R2 = 1-pyrrolidinyl) and which included a metathesis ring closure of the corresponding N-allyl-amide, R2SO2-3-C6H4CH(CH2CH:CH2)CON(CH2CH:CH2)CH(Ph)CH2R2 (R2 = 1-pyrrolidinyl ). The prepd. lactams were assayed for analgesic activity and for μ-, δ- and κ- opioid receptor binding activity.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:863130 CAPLUS
DN 142:56151
TI Azepinone as a conformational constraint in the design of κ-opioid receptor agonists
AU Tuthill, Paul A.; Seida, Pamela R.; Barker, William; Cassel, Joel A.; Belanger, Serge; DeHaven, Robert N.; Koblish, Michael; Gottshall, Susan L.; Little, Patrick J.; DeHaven-Hudkins, Diane L.; Dolle, Roland E.
CS Adolor Corporation, Department of Chemistry, Exton, PA, 19341, USA
SO Bioorganic & Medicinal Chemistry Letters (2004), 14(22), 5693-5697
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 142:56151
GI



I

AB A new class of κ- opioid receptor agonists is described. The design of these agents was based upon energy minimization and structural overlay studies of a generic azepin-2-one structure with the crystal structure of arylacetamide κ agonist ICI 199441. The most active compound identified was ligand (3S)-3-(3,4-dichlorophenyl)-1,3,4,7-tetrahydro-1-[(1S)-1-phenyl-2-(1-pyrrolidinyl )ethyl]-2H-azepin-2-one (I) (Ki = 0.34 nM), which demonstrated potent antinociceptive activity after oral administration in rodents.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     (FILE 'HOME' ENTERED AT 15:10:17 ON 02 AUG 2006)

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               S L1

     FILE 'REGISTRY' ENTERED AT 15:10:50 ON 02 AUG 2006
L*** DEL       0 S L1

     FILE 'CAPLUS' ENTERED AT 15:10:51 ON 02 AUG 2006
L*** DEL       0 S L2

     FILE 'REGISTRY' ENTERED AT 15:11:27 ON 02 AUG 2006
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L3            62 SEA SSS FUL L1

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                 D 1-12 BIB ABS HITSTR
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L5           174 SEA ABB=ON  PLU=ON  ("DOLLE ROLAND E"/AU OR "DOLLE ROLAND E
                 III"/AU OR "DOLLE ROLAND E JR"/AU OR "DOLLE ROLAND ELLWOOD"/AU
                 OR "DOLLE ROLAND ELLWOOD III"/AU)
                 E CHU GUO HUA/AU
L6            27 SEA ABB=ON  PLU=ON  "CHU GUO HUA"/AU
                 E GU MINGHUA/AU
L7            12 SEA ABB=ON  PLU=ON  "GU MINGHUA"/AU
L8           196 SEA ABB=ON  PLU=ON  L5 OR L6 OR L7
L9            31 SEA ABB=ON  PLU=ON  L8 AND OPIOID
L10            8 SEA ABB=ON  PLU=ON  L9 AND PYRROLID?
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                 D 1-8 BIB ABS


     FILE HOME

     FILE CAPLUS

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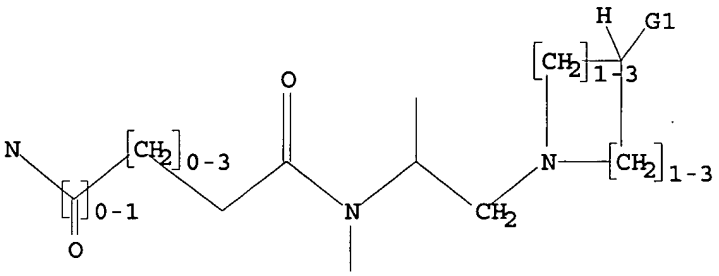
L1 STR




G1 H,OH

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L4 12 SEA FILE=CAPLUS ABB=ON PLU=ON L3

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